EXHIBIT I

Our Case No. 10709/47

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
Zheng Wei	
Serial No. 10/630,180	Examiner: DeBerry, Regina M.
Filing Date: July 30, 2003	Group Art Unit No. 1647
For: METHOD FOR MULTIPLE CHEMOKINE RECEPTOR SCREENING FOR ANTAGONISTS USING RAM ASSAY	Confirmation No. 9214

DECLARATION OF ZHENG WEI UNDER 37 C.F.R. § 1.132

I, Zheng Wei, Ph.D., declare that:

1. I received my B.A. in Biology in 1985 from South China Normal University and my Ph.D. in Biochemistry and Molecular Biology from the University of California at Davis in 1999. I was at ChemoCentryx, Inc. from 1998 to 2007.

2. I am the sole named inventor of the above-identified patent application ("the '180 application"). I have read the Office Action mailed February 7, 2008 in the '180 application.

3. BiRAM assay is a screen assay where two types of chemoattractant receptors are assayed simultaneously in the same assay.

4. MultiRAM assay is a screen assay where multiple types of chemoattractant receptors are assayed simultaneously in the same assay.

5. The BiRAM and MultiRAM assays can be efficiently used to quickly identify potential antagonists for the chemoattractant receptors from a large pool of compounds with unknown antagonist activity.

6. Specifically, in the BiRAM or MultiRAM assay, numerous compounds can be simultaneously screened for their ability to cause cell migration in the presence of the inhibitory concentrations of ligands for the chemoattractant receptors. The BiRAM and MultiRAM assays can be performed in two ways. A single cell population including two types of chemoattractant receptors is placed in the upper chamber of the apparatus. Alternatively, two cell populations, where the first cell population includes one type of chemoattractant receptor and the second cell population includes another type of chemoattractant receptor, is placed in the upper chamber of the apparatus. An inhibitory concentration of a ligand for the first chemoattractant receptor and an inhibitory concentration of a ligand for the second chemoattractant receptor are placed in the lower chamber. The movement of the cell population(s) from the upper chamber to the lower chamber is then monitored. If cell movement is caused by any particular candidate antagonist(s) tested in the assay, the candidate antagonist(s) is identified as an antagonist of at least one of the two types of chemoattractant receptors expressed by the cells. Specific details of the BiRAM and MultiRAM assays are provided in the '180 application.

7. In Example 8, I validated BiRAM assay using *known* antagonists of CCR1 and CCR2 chemoattractant receptors, both of which were expressed on a

single population of the THP-1 cells. I was able to demonstrate that the BiRAM assay efficiently screened antagonists for CCR1 and CCR2 chemoattractant receptors expressed on the THP-1 cells by confirming that the tested compounds were, in fact, antagonists of the CCR1 and/or CCR2 receptors.

8. Hereon I describe experiments were I repeated the experiments described in Example 8 using 92 *unknown* compounds (i.e., candidate antagonists).

9. In the experiment, I used THP-1 cells expressing CCR1 and CCR2 chemoattractant receptors and inhibitory concentrations of MIP1α and MCP1, which are ligands for CCR1 and CCR2, respectively. Two samples containing 1nM of MCP1, which is a known ligand of CCR2 receptor, were used as a positive control for CCR2 receptor. Also, two other samples containing 0.5nM of MIP1α, which is a known ligand for CCR1 receptor, were used as a positive control for CCR1 receptor.

10. In short, THP-1 cells expressing CCR1 and CCR2 chemoattractant receptors were used in the assay. The THP-1 cells and 10μM of each test candidate antagonist (92 samples) were placed in the upper chamber of a cell migration apparatus. Inhibitory concentrations of the ligands for the CCR1 and CCR2 receptors, MCP1 and MIP1α, respectively, were placed in the lower chamber of the cell migration apparatus. I have previously shown that the inhibitory concentrations of MCP1 and MIP1α inhibit cell migration of THP-1 cells that express CCR1 and CCR2 receptors.

11. Following incubation, as described in Example 8, the BiRAM assay was terminated and the THP-1 cells that migrated to the lower chamber of the cell migration apparatus in response to the antagonist compounds were quantified by CyQuant assay.

12. Exhibit A illustrates data obtained from the BiRAM assay described above designed to simultaneously test at least 92 test candidate antagonists on a 96 well plate.

13. As shown in the top panel of Exhibit A, a 'hit' antagonist, CMP2145, was identified using the BiRAM assay. The CMP2145 compound was recognizable from its enhanced signal over the background. The positive controls (i.e., MCP1 and MIP1α) are also marked in the figure.

14. As shown in the bottom panel of Exhibit A, RAM index (RI) was calculated by dividing the signal for each of the test compounds by the average signal of the 92 test wells. The CMP2145 compound was identified as a potential antagonist of either the CCR1 or CCR2 chemoattractant receptor.

15. Thus, the BiRAM assay was used to quickly narrow a field of 92 possible antagonists to a single candidate.

16. To determine whether the CMP2145 compound is an antagonist of CCR1 or CCR2, the CMP2145 was further assayed in a conventional migration assay, similar to one described in Example 1 at pages 32-33 of the '180 application.

17. THP-1 cells expressing CCR2 receptor were then exposed to 0.1nM MCP1 in the presence of serially-diluted 'hit' antagonist, CMP2145.

18. Exhibit B is a figure generated from data obtained from the conventional migration assay described above. As shown in the figure, CMP2145 was able to inhibit the MCP1-induced cell migration of the THP-1 cells expressing the CCR2 receptor. As such, CMP2145 was identified as the antagonist of the CCR2 chemoattractant receptor.

19. The CMP2145 compound was also tested in another conventional migration assay using THP-1 cells expressing CCR1 receptor and MIP1α. The CMP2145 did not inhibit the MIP1α-induced cell migration of THP-1 cells expressing the CCR1 receptor (data not shown). As such, CMP2145 was not identified as an antagonist of CCR1 chemoattractant receptor.

20. It is my opinion and belief that in addition to convention cell migration assays, uniRAM or a calcium immobilization assays may also have been used to identify the receptor that the CMP2145 compound was inhibiting.

21. In summary, I was able to simultaneously test 92 possible antagonist compounds in a single BiRAM assay and quickly identify one compound out of the 92 screened compounds being tested as an the antagonist of the CCR1, CCR2, or both, which I then confirmed using a conventional migration assay to be an antagonist of only the CCR2 receptor.

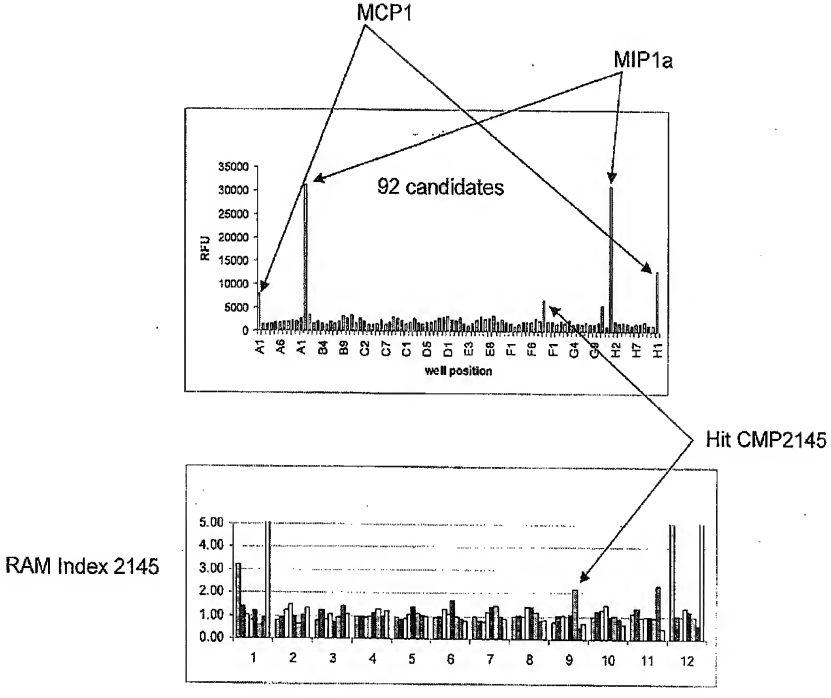
22. I have also used the MultiRAM assay to similarly simultaneously test numerous possible candidate antagonists in a single assay (data not shown).

23. I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on knowledge and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements, and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the U.S. Code and that such willful false statements may jeopardize the validity of the patent application or any patent issuing thereon.

July 23, 2008
Date

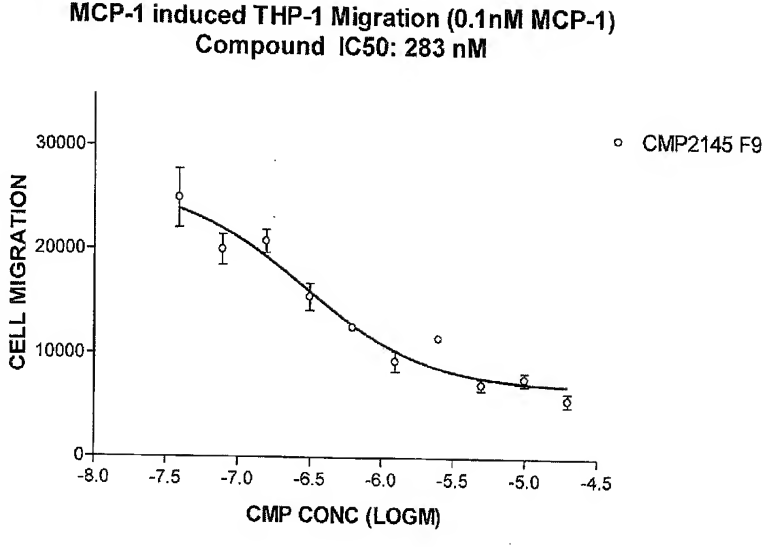
Zheng Wei

Exhibit A



- Testset: biRAM 16b

Exhibit B


MCP-1 induced THP-1 Migration (0.1nM MCP-1)
Compound IC50: 283 nM
CELL MIGRATION
30000
20000
10000
0
-8.0
-7.5
-7.0
-6.5
-6.0
-5.5
-5.0
-4.5
CMP CONC (LOGM)
CMP2145 F9